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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,001	11/03/2005	Tetsu Akiyama	3190-078	7470

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KILYK & BOWERSOX, P.L.L.C.  
400 HOLIDAY COURT  
SUITE 102  
WARRENTON, VA 20186

EXAMINER

SHIN, DANA H

ART UNIT PAPER NUMBER

1635

DATE MAILED: 05/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/537,001	Applicant(s) AKIYAMA ET AL.	
	Examiner Dana Shin	Art Unit 1635	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 20 May 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-25 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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## DETAILED ACTION

### *Election/Restrictions*

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted as below:

Group I, claim(s) 1, 26, 33-34 (in part), 37-38, and 42-43, drawn to an agent for inhibiting metastasis of colorectal cancer, wherein the agent inhibits the expression of Asef.

If this group is elected, applicants are further required to elect one oligonucleotide sequence from SEQ ID NOS:1 and 3 as set forth in claim 38. Note this is not a species election.

Group II, claim(s) 33-34 (in part), 37, 39, 42-43, and 48, drawn to an agent for inhibiting metastasis of colorectal cancer, wherein the agent inhibits the expression of APC.

If this group is elected, applicants are further required to elect one oligonucleotide sequence from SEQ ID NO:2 and 4 as set forth in claim 39. Note this is not a species election.

Group III, claim(s) 1 and 27, drawn to an agent for inhibiting metastasis of colorectal cancer, wherein the agent inhibits the binding of Asef to the gene product of APC.

Group IV, claim(s) 1 and 28, drawn to an agent for inhibiting metastasis of colorectal cancer, wherein the agent inhibits the guanine nucleotide exchange factor activity of Asef.

Group V, claim(s) 29-30, 35-36 (in part), 40-41, 44-47 and 50, drawn to a method for inhibiting metastasis of colorectal cancer, wherein the method comprises inhibiting the expression or function of the Asef of claim 38

If this group is elected, applicants are further required to elect one oligonucleotide sequence from SEQ ID NOS: 1 and 3 as set forth in claim 38. Note this is not a species election.

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Group VI, claim(s) 35-36 (in part), 41, 44, 49, and 51 drawn to a method for inhibiting metastasis of colorectal cancer, wherein the method comprises using the agent that inhibits APC.

If this group is elected, applicants are further required to elect one oligonucleotide sequence from SEQ ID NOs: 2 and 4 as set forth in claim 41. Note this is not a species election.

Group VII, claim(s) 29 and 31, drawn to a method for inhibiting metastasis of colorectal cancer, wherein the method comprises inhibiting the binding of Asef to the gene product of APC.

Group VIII, claim(s) 29 and 32, drawn to a method for inhibiting metastasis of colorectal cancer, wherein the method comprises inhibiting the guanine nucleotide exchange factor activity of Asef.

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The inventions of groups I-VIII are found to have no special technical feature that define a contribution over the prior art of Kawasaki et al. (Science, Vol. 289, pp 1194-7, 2000), in view of Senda et al. (Biochemical And Biophysical Research Communications, Vol. 223, pp 329-34, 1996). The special technical feature of the first claimed invention is an agent that inhibits the expression of Asef, which in turn inhibits metastasis of colorectal cancer.

Reference of Kawasaki et al., teaches that Asef interacts *in vivo* with the armadillo repeat domain of APC and that APC and ASEF colocalize in mouse colon epithelial cells. Furthermore, it teaches that ASEF, APC, and beta-catenin are found in the same complex *in vivo*, which may regulate the actin cytoskeletal network, cell morphology and migration. Reference of Senda et al., teaches that APC is a tumor suppressor protein that colocalizes with beta-catenin in colon epithelial cells. Taken together, the combined teachings of above prior art suggest that Asef, via

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*in vivo* interaction with APC and beta-catenin, may regulate cellular processes in colon epithelial cells and that it may be advantageous to inhibit function/expression of Asef to interfere with the regulatory roles of Asef in cellular processes in the colon epithelium, which contemplates an agent that inhibits the expression of Asef. Therefore, applicants' invention of the agent for inhibiting metastasis of colorectal cancer via inhibiting Asef does not contribute a special technical feature when viewed over the prior art. Accordingly, they do not have a single inventive concept and so lack unity of invention, thus restriction for examination purposes as indicated is proper.

According to the guidelines in Section (f)(i)(a) of Annex B of the PCT Administrative Instructions, the special technical feature as defined by PCT Rule 13.2 shall be considered to be met when all the alternatives of a Markush-group are of similar nature. For chemical alternatives, such as the claimed polynucleotide target sequence regions, the Markush group shall be regarded as being of similar nature when

(A) all alternatives have a common property or activity and

(B)(1) a common structure is present, i.e, a significant structure is shared by all of the alternatives or

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to an art recognized class of compounds in the art to which the invention pertains.

The instant oligonucleotide sequences are considered to be each separate invention for the following reasons:

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As described above, the oligonucleotide sequences do not meet the criteria of (A), common property or activity or (B)(1), common structure or (B)(2), art recognized class of compounds. Although all oligonucleotide sequences are designed to inhibit expression of a gene, each sequence behaves in a different way in the context of the claimed invention because each region comprises different nucleic acid sequences that constitute a particular region of an mRNA. Moreover, SEQ ID NOs: 1 and 3 target the Asef gene while SEQ ID NOs: 2 and 4 target the APC gene as evident in the sequence listing filed on May 20, 2005. Therefore, each sequence region cannot be substituted one for the other, with the expectation that the same intended result would be achieved. Further, although the oligonucleotide sequences of SEQ ID NOs: 1 and 3 or SEQ ID NOs: 2 and 4 disclosed in the claims may interact with the mRNA of Asef or APC, respectively, the sequence regions do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure. Accordingly, unity of invention between the sequence regions is lacking and each agent claimed is considered to constitute a special technical feature. Therefore, applicants are required to elect two target sequence regions as indicated above.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

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Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

### ***Inventorship***

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

### ***Conclusion***

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

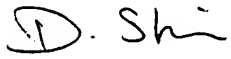
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

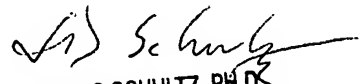
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Dana Shin  
Examiner  
Art Unit 1635

  
5-15-2006

  
JAMES SCHULTZ, PH.D.  
PRIMARY EXAMINER